VITAMIN D STATUS AND SUNSCREEN USE

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THE IMPORTANCE OF VITAMIN D

Vitamin D and its relationship to a wide number of illnesses and health parameters is presently one of the most discussed topics in medical and nutritional literature. It seems there are few, if any, diseases to which vitamin D deficiency is not related. A large number of articles in the medical literature were reviewed for discussion in this article. The best effort was made to present the current evidence in a systematic and usable fashion. At the same time, it must also be emphasized that, due to present immense interest in this topic, many more studies are still being conducted. Future knowledge will be gained from these investigations and, as is usually the case with scientific inquiry, modifications will probably occur in terms of present recommendations. However, it is clear that the effect of vitamin D levels on the incidence of numerous diseases and even on simple feelings of well-being has been greatly underestimated in the past.

HUMAN METABOLISM OF VITAMIN D

We think only plants photosynthesize, but humans also photosynthesize vitamin D in skin after UVB rays in sunlight strike the epidermal surface. One would think that sunscreen application would prevent the formation of vitamin D in skin. Some studies have shown this decrease in vitamin D with sunscreen use, but most have not. This may be related to the public using lower amounts of sunscreen than recommended and also lower than the amounts used to determine the SPF of the sunscreen. If education encourages the public to begin using more appropriate amounts of sunscreen, a further drop in the average levels of serum vitamin D could be seen. When the SPF of sunscreen is compared to its efficiency in inhibiting the formation of vitamin D, sunscreens are actually much more efficient at blocking vitamin D production than they are at preventing sunburn. Heavily pigmented individuals living at higher altitudes with lower sun exposure are at particular risk for decreased vitamin D levels. Persons with darker skin are now being encouraged to use sunscreen to decrease risks of sun exposure, particularly skin cancer, although the addition of sunscreen could cause their vitamin D levels to be even lower.

Vitamin D is one of the fat-soluble vitamins, along with A, E and K. Because it is stored in fat, high intakes of vitamin D can theoretically lead to toxicity. However, in the studies reviewed, the only adverse effect found was a very minimal risk in the frequency of kidney stones when taking both calcium and vitamin D. Also, the other health benefits of the supplementation far outweighed this risk. As stated in the British Journal of Dermatology (2009 Nov;161 Suppl 3:54-60) "most experts in the field agree that the evidence to date suggests that daily intake of 1000-2000 IU vitamin D could reduce the incidence of vitamin D-deficiency-related diseases with minimal risk in Europe, the US, and other countries."

There are 2 forms of vitamin D, ergocalciferol or D2 and cholecalciferol or D3. D2 is primarily found in plants and D3 in animals. In humans, D3 can be synthesized in the skin when its chemical precursor is exposed to sunlight or ingested from animal sources, although animal tissue provides only a very small amount. An exception to this is fatty wild-caught fish such as tuna, mackerel, herring and sardines which contain a fair amount of the vitamin. Farmed fish contains inadequate amounts of vitamin D. Some foods, as milk and cereal, have added vitamin D but, once again, this amount is very inadequate. D3 and D2 are both converted in the liver to 25-hydroxy-vitamin D, the primary circulating form. Conversion into the active form, 1,25-dihyroxy-vitamin D occurs in the kidney.

Vitamin D's main role is to regulate levels of calcium and phosphorus with respect to building and repairing bone.

Vitamin D encourages the absorption of both calcium and phosphorus from food in the small intestine.

VITAMIN D AND ILLNESS

Low levels of vitamin D are associated with the occurrence of many health problems worldwide. These include cardiovascular disease, immune deficiency (including severe infections as pneumonia, tuberculosis susceptibility, and milder viral infections such as colds and influenza), internal cancers (including breast, ovary, prostate, Hodgkins's lymphoma, non-Hodgkin's lymphoma, colon), dementia, bone health (including osteoporosis, osteomalacia, rickets), psoriasis, diabetes mellitus, hypertension, myopathies (muscle diseases), multiple sclerosis, mental illness (including depression, schizophrenia), autoimmune disease, dementia and other forms of cognitive decline. Poor serum vitamin D levels are associated with poorer physical performance and greater rate of decline in older persons.

Low levels in pregnant females have been associated with increased risk of infant disease. The onset of schizophrenia later in life is associated with low maternal levels of vitamin D during pregnancy. This may be especially important in migrant black children living at high altitudes as there is also a particularly high incidence of schizophrenia in this population group. Interestingly, unusually high levels of vitamin D in infants are also associated with risk of schizophrenia. The authors postulated that in this group with high levels of D there might be an inability to metabolize the vitamin also resulting in an overall deficiency state.

There is a tendency in medical studies to focus on severe deficiency states only, and vitamin D levels within the deficient range are definitely associated with the occurrence of many diseases. Criticism is often levied at these types of studies, however, in that they imply a "low but not severely deficient" level of a nutrient is acceptable when this may not be the case. Studies are often not done to determine the level of a nutrient supportive of optimum health rather than only the absence of disease. Many medical studies therefore criticize the current dietary recommendations of vitamin D, saying they are inadequate – and especially so during pregnancy and lactation.

Evidence from smaller regions within a country or geographic area have shown that regional variations in vitamin D levels correlate with decreased disease resistance and/or impaired response to disease treatment. In Norway, a number of cancers have been analyzed with respect to vitamin D levels. Breast cancer has a better prognosis if diagnosed in summer or autumn when serum vitamin D levels are higher. Three-year survival of colon cancer and prostate cancer patients in Norway is higher with seasonal increases in vitamin D levels. There is a beneficial effect of summer season or high vitamin D intake with outcome for lung cancer in Norway.

When very strict statistical criteria are applied, the strongest evidence that vitamin D reduces the risk of cancer exists for breast, colon and rectal cancers. There is also good evidence in this regard for bladder, esophageal, gallbladder, stomach, ovarian, renal and uterine cancer. Although there are mixed statistical findings for pancreatic, prostate cancer and melanoma, the benefit of vitamin D in helping to prevent these cancers is also reasonably strong. Considering the many effects of vitamin D on factors effecting cancer growth in general, it is not surprising that benefits are seen in so many cancers accompanying higher levels of vitamin D. This vitamin suppresses invasion of tissues by the malignancy, and inhibits metastasis and angiogenesis (new blood vessel formation required for tumor growth). Women in the United States with decreased vitamin D levels have a 253 percent risk increase for developing colorectal cancer.

Most studies claim a definite association between vitamin D levels and bone health, including osteoporosis, falls, fracture risk and bone mineral density. Some studies indicate that the evidence is best for older children and adults and inconsistent in younger children and infants. However, most of the international studies, particularly in underdeveloped areas or in more severe deficiency states, found a stronger association

between vitamin D levels and bone health in young children and infants. The Women's Health Initiative, a very large study of 68,132 postmenopausal women has been analyzed for hip fracture prevention with the use of calcium and vitamin D supplementation. Interestingly, no evidence of protection was found. There also was no association with vitamin D levels and systolic blood pressure, cardiovascular disease, overall mortality, cognitive defects or depression. However, the dose of vitamin D given in the WIH was only 400 IU daily which was lower than in most studies. Many other studies using moderate doses found improvements in bone health and the other parameters listed with vitamin D supplementation.

EPIDEMIOLOGIC (POPULATION) STUDIES

Large studies have been conducted in several countries to determine if taking additional vitamin D orally would decrease disease incidence and save on healthcare costs. These calculated cost savings and other data are listed below by country.

Canada—decrease annual death rate by 37,000—$14.4 billion savings

Europe—€177,000 million annual savings after paying for costs of education and testing levels of serum vitamin D

United States—cancer savings alone of $16-25 billion annually (dose of 1000 IU daily)—decrease 4-year overall risk of developing cancer in women by over 60% (dose of 1500 IU daily)

PERSONS AT RISK FOR VITAMIN D DEFICIENCY

Estimates of US adults and adolescents who are deficient in vitamin D range from 21 to 58%. At least 54% of homebound adults are deficient.

Persons who avoid sun exposure are at risk for low levels of vitamin D. Individuals with problems such as systemic lupus may avoid the sun since it causes their rash to worsen. Obese and elderly persons may avoid sun exposure. Any other mechanism that decreases solar exposure will decrease levels of vitamin D. Clothing effectively blocks all vitamin D production. Persons who use sunscreen, particularly in the proper amounts to protect from skin cancer and photoaging, are at risk for low vitamin D. Use of "sunless tanners" which contain dihydroxyacetone-induced melanoidins also decrease vitamin D synthesis.

Obese persons have lower levels of vitamin D. At first this was thought to be related solely to decreased time in the sun but when obese persons who sunbathe are evaluated, they too have lower vitamin D levels.

Persons with chronic kidney disease and those on dialysis have lower vitamin D levels. This is because they live mostly indoors and in addition, due to diseased kidneys, have impaired production of the active form of the vitamin.

The aged are at increased risk for deficient vitamin D status. They have decreased sun exposure, often inadequate dietary intake and, secondary to metabolic decline, have impaired synthesis of vitamin D at all levels in the body.

Darker-skinned individuals with more melanin in their skin have lower vitamin D levels.

Living in a sunny area does not assure a healthy level of vitamin D. In fact, low levels of vitamin D are pervasive in all geographic areas, including heavily sun-exposed locations. Ten percent of persons in Queensland had levels below 25 nmol/liter – which is a level considered to be definitely deficient. Thirty-two percent of this same population had slightly higher but still insufficient levels. Levels were even lower in darker-skinned individuals in this population compared to fair-skinned.

Asian women were studied in 1999 and found to have adequate D levels in spite of age. They lived in a rural community, however, and may have spent more time outside. There also may be other unknown factors involved in their adequate levels.

Patients having had organ transplants are strongly

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SUNSCREEN STUDY

erythema reduction study

UV PROTECTION AND ERYTHEMA REDUCTION

STUDY OBJECTIVE The safety and effectiveness of INNOVATIVE SKINCARE® SPF 25 TREATMENT SUNSCREEN in preventing solar damage and reducing erythema in individuals exposed to the full spectrum of UVA and UVB rays were evaluated.

STUDY DESIGN SPF 25 TREATMENT SUNSCREEN was examined under stringently controlled laboratory conditions enforced by the FDA. Test subjects with Fitzpatrick skin types I, II and III (those who burn most easily from sun exposure) were exposed to the full spectrum of UVA and UVB rays. Exposure of up to 2.5 times the amount that produced erythema (redness) was used in each subject. Each subject was assessed at 24, 48 and 72 hours post-exposure.

Additionally, test subjects were treated with SPF 25 TREATMENT SUNSCREEN immediately after exposure to UVA and UVB rays. Exposure of up to 2.5 times the amount that produced erythema (redness) was used in each subject. Each subject was assessed at 72 hours post-exposure.

The test situation was designed to cause solar damage in the subjects in order to provide a complete assessment of the product's effectiveness.

SIGNIFICANCE OF STUDY Proper sun protection is an essential element of any skincare regime. Selecting a Sun Protection Factor is of utmost importance. In clinical studies, sunscreens with an SPF over 30 have been found to provide little more protective ability than those under 30, and are associated with much more frequent user side effects. Protecting from harmful UV radiation is only the first step. Protecting against inflammation and oxidative stress caused by UV radiation is also an important aspect to more comprehensive sun protection.

RESULTS AND CONCLUSIONS When INNOVATIVE SKINCARE® SPF 25 TREATMENT SUNSCREEN was applied 15 minutes before exposure, the development of redness, swelling and blistering was completely prevented in all subjects. In the control subjects (those applying no sunscreen), redness, swelling and blistering occurred as expected from exposure to UVA and UVB rays.

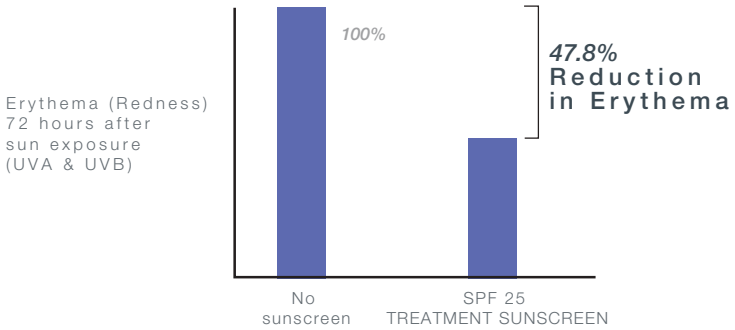
SPF 25 TREATMENT SUNSCREEN exhibited an actual SPF value of 26. Sunscreens with an SPF over 30 are frequently associated with inflammation, irritation and rash that can last for weeks even though they provide an insignificant amount of additional protection against the damage caused by sun exposure. No adverse reactions were reported in any subject as the result of using this product and sun protective ability was excellent. SPF 25 TREATMENT SUNSCREEN provides a safe balance between UVB protection and user side effects.

It is already known that long-term effects of solar damage also occur in those with darker complexions. Therefore, sunscreen use is recommended in ALL Fitzpatrick skin types.

When INNOVATIVE SKINCARE® SPF 25 TREATMENT SUNSCREEN was applied to the skin of the test subjects immediately after UVA and UVB exposure, there was a 45-53 percent reduction (distributive mean of 47.8 percent reduction) in skin damage over the 72 hour period after exposure.

In summary, in FDA-monitored clinical studies, INNOVATIVE SKINCARE® SPF 25 TREATMENT SUNSCREEN was found to be both safe and effective. It not only provides excellent protection from UV damage, but also simultaneously and effectively reduces the internal damage associated with sunburn. In fact, this product is so successful in reducing erythema, that it may also be used as a sunburn treatment – a first in the sun protection field.

ERYTHEMA REDUCTION



INNOVATIVE SKINCARE® SPF 25 TREATMENT SUNSCREEN
applied 15 minutes after sun exposure

UV DAMAGE EFFECTS

- Collagen breakdown
- Diminishment of DNA repair
- Free radical damage
- Immune system suppression
- Cellular death/apoptosis
- Pigmentation changes
- Pre-cancerous lesions

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THE NEW EXTREME PROTECT SPF 30 SUNSCREEN™

repared by Charlene eaven, , AC , Clinical irector

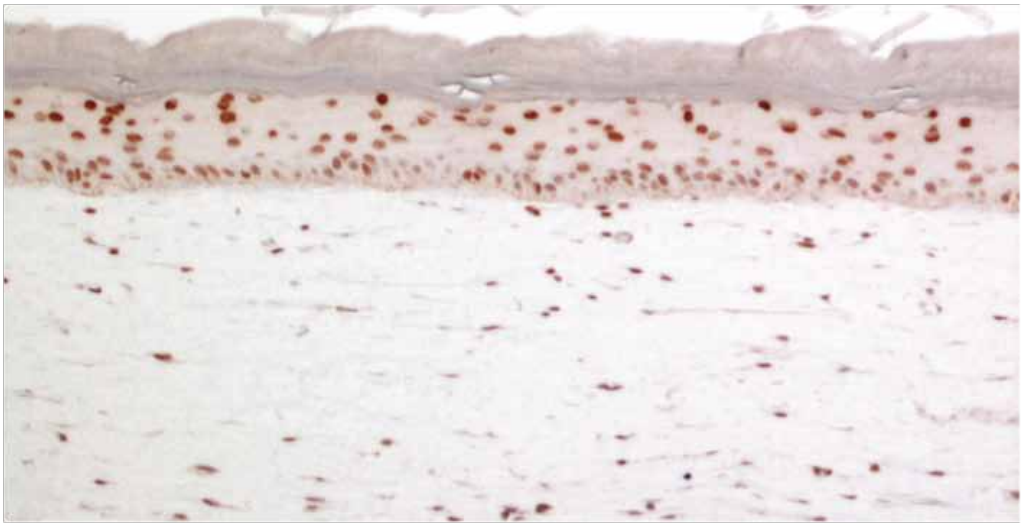
Skin ages from both the creation of energy within cells called intrinsic free radical damage as well as bombardment by the sun s rays called photoaging. hese processes attack and in ure cellular proteins. Skin contains the highest amount of collagen found anywhere in the body and collagen is the body s most numerous protein. C S 0 SU SC repairs collagen damage that would otherwise lead to wrinkled sun damaged skin.

Another effect of sun exposure and aging is A damage and its increased risk of cancer. Solar rays damage the A of the chromosomes within the nucleus of every skin cell. Since A is the genetic material responsible for directing the cell in proper functioning, improper messages are given and health declines. As A damage extends further, cancer develops.

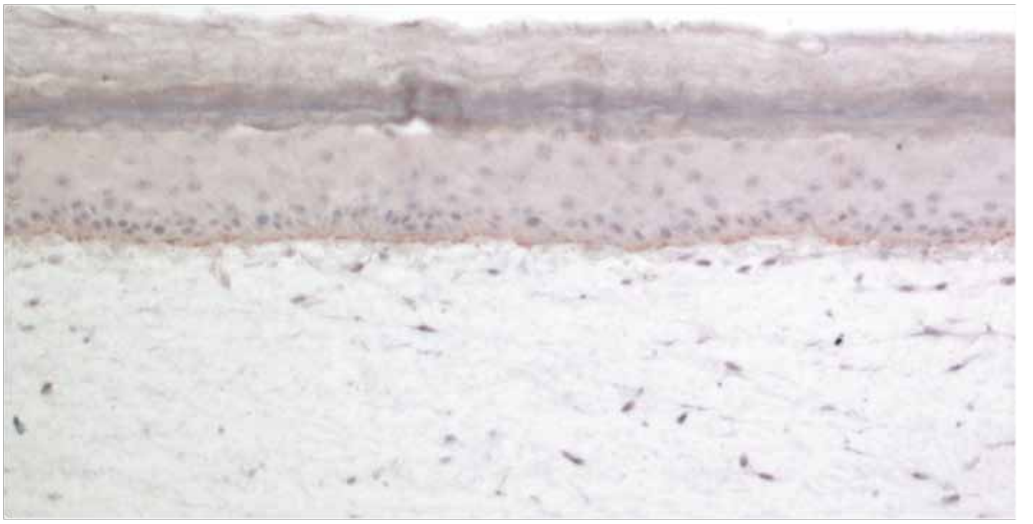
hymine dimers, measurements of A damage, increase with sun exposure. igh thymine dimers indicate high risk of skin cancer. Skin protected with C S 0 SU SC was exposed to solar radiation containing both U A and U rays. Under these experimental conditions, thymine dimers were produced. Skin exposed to solar rays but without C S 0 SU SC contained large amounts of thymine dimers consistent with high cancer risk. urthermore, the C SU SC even prevented thymine dimer formation from ongoing cellular metabolism.

ew C S 0 SU SC is designed to protect and preserve healthy skin against environmental stress, sun exposure and aging. t contains extremo ymes, en ymatic systems developed by organisms able to survive in the most extreme environments on earth. any extremo ymes work via antioxidant mechanisms and others work by protecting proteins and other biologics through other uni ue ways. C S 0 SU SC borrowed from nature the biochemical defense mechanisms of these plants and applied them to the principles of skin defense against sun exposure and aging. xtremo ymes are tremendously powerful systems specifically designed by nature for environmental protection in environments of extreme exposure.

In the photo below skin exposed to the sun's rays was examined under a microscope. The brown areas are cells containing thymine dimers and damaged DNA. The arrow points to the epidermis where these cells are easily seen. The photograph illustrates considerable cancer risk.



In the next experiment shown below, [illegible] was applied to the skin before sun exposure. No brown cells can be seen in the epidermis, indicating complete protection from DNA damage. The arrow points to the important layer where no thymine dimers were found when [illegible] was used.



In summary, [illegible] shelters healthy collagen from sun exposure and aging. It contains powerful DNA protectants that combat the tendency toward skin cancer caused by sun damage. It maintains and preserves healthy skin even during environmental exposure and aging.

ADVANCEMENT IN DNA REPAIR ENZYMES: EXTREMOZYMES®

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EXTREMOZYMES AND EXTREMOPHILES

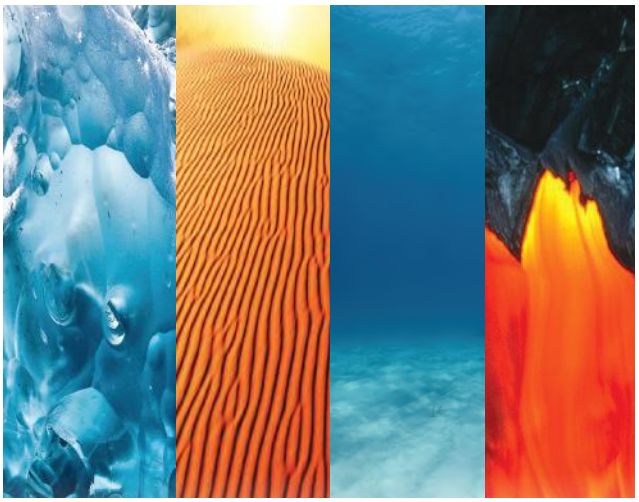
Extremozymes are enzymes developed by plants living in extreme environments that assist survival and adaptability. Organisms able to not only survive but thrive in harsh planetary locations are called "extremophiles", a term that literally means "extreme loving." Scientists have been fascinated with extremophiles for many years and have studied their adaptive mechanisms.

Many of these extremophiles are micro-organisms, but even more complex organisms, such as plants, have been able to adapt to the extent required to survive at planetary extremes. These organisms, some of which date back more than 40 million years, use powerful biologic processes to protect themselves against extreme cold, heat, salinity, pH balance, dehydration and radiation.

Varieties of extremophiles include hypoliths from cold, dry deserts; cryophyles found in polar ice; piezophiles from pressurized deep ocean trenches; thermophiles from very hot areas; and polyextremophiles from environments containing multiple adversities. A number of polyextremophiles originate from marine environments where there may be extremes of temperature, pressure, salinity and darkness.

EXTREMOZYMES IN NATURE

Extremophiles have developed a variety of ingenious survival strategies allowing them to regenerate, metabolize and reproduce in spite of very difficult environmental conditions. Their enzyme systems, Extremozymes, protect vital biological macromolecules, cells and chromosomal DNA from damage by external stresses. In addition to protein structural components, an organisms's DNA genetic blueprint is one of the most important elements that every organism must conserve for survival. Methods of protection include unique configurations of protein folding, protection from dehydration by incorporation of sugar molecules, and biochemical means of cushioning and shielding DNA. An example of this ability is prevention of thymine dimer formation when DNA is exposed to oxidative stress and radiation in these extreme environments. These unique, natural enzymes scavenge free radicals and destroy radical oxygen species.

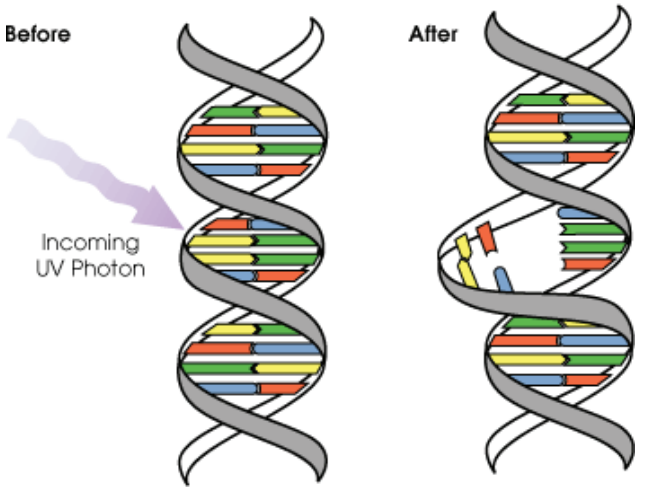


Some of the harsh environments in which extremophiles thrive include extreme cold, heat, dryness, and deep ocean trenches.

EXTREMOZYMES FOR SKIN

Human skin also experiences environmental extremes. The power of Extremozymes may be harnessed for skin protection against environmental damage including dryness, wind, radiation (solar UVA and UVB), heat, cold, salinity (saltiness from sweating) and irritation (e.g. from soaps). Exposure of structural proteins including collagen and elastin to moisture loss, radiation, heat, cold, and free radical damage as well as exposure of essential genetic DNA to environmental stresses causes aging with loss of elasticity, resilience, immune function, and cancer resistance.

Exposure of skin to solar rays causes photoaging. Thymine dimers form abnormal cross-bridges in DNA as intranuclear DNA experiences oxidative stress. Measurement of thymine dimers as well as other DNA damage markers such as sunburn cell formation can be measured scientifically. Quantification of thymine dimer and sunburn cell formation is a key parameter of sun damage. Just as Extremozymes® shield extremophilic organisms from damaging environmental radiation, the ravages of solar radiation on skin can be lessened by incorporating Extremozymes technology into skin care.



UV Radiation causes the formation of thymine dimers, a form of DNA damage.

The genetic adaptations of extremophiles and their Extremozymes have profound functional applications to skin care. Over time, environmental conditions have a very noticeable and disastrous effect on our skin. Nature's miracles of adaptation can also be used to protect human skin from damage caused by environmental extremes. INNOVATIVE SKINCARE® has drawn from the natural selection processes of specialized extremophilic organisms, pioneering the future of skin care in terms of ultimate protection for healthy skin.

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INNOVATIVE SKINCARE®

EXTREME PROTECT® SPF 30

7.9 pH +/- 0.5 100g £60

PROTECTS I REPARATIVE I ANTI-AGING

EXTREME PROTECT SPF 30 shelters healthy collagen from sun exposure and aging. It contains powerful DNA protectants that combat the tendency toward skin cancer caused by sun damage. It maintains and preserves healthy skin even during environmental exposure and aging. EXTREME PROTECT SPF 30 Provides broad-spectrum UVA/UVB protection for the ultimate in protection and is proven to help protect against skin damage; this elegant, moisturizing sunscreen also helps repair solar damage by reducing redness and inflammation associated with sunburn. Microfine zinc oxide and micro-encapsulated sunscreens are combined with powerful botanical Extremozyme® antioxidants to offer the most advanced protection available.

BENEFITS

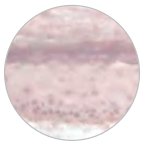
- Provides broad spectrum UVA/UVB protection
- Protects & repairs collagen and cell DNA
- Diminishes appearance of fine lines & wrinkles
- Hydrates, smoothes & softens
- Provides antioxidant rich protective barrier

CLINICAL TEST RESULTS

UNPROTECTED

Photomicrograph after sun exposure – brown areas are cells containing thymine dimers and damaged DNA indicating considerable cancer risk.

PROTECTED



Extreme rotect spf 30 applied before sun exposure indicates virtually no thymer dimers in the epidermis and near complete protection from DNA damage.

PRODUCT HIGHLIGHTS

“EXTREMOZYME® TECHNOLOGY

INNOVATIVE SKINCARE®’S breakthrough Extremozyme® technology features advanced formulations of highly specialized enzymes developed via natural selection to allow micro-organisms to survive in extreme environments of pressure, heat, cold, dryness, salt, pH, and radiation. These unique enzymes, called “Extremozymes”, protect cells and biological macromolecules from damage by external stresses which helps PROTECT and REPAIR your skin in an unprecedented and exceptional manner.

KEY INGREDIENTS	INGREDIENT BENEFITS
OCTINOXATE (organic encapsulated) 5.5%	Provides broad-spectrum sunscreen protection.
ZINC OXIDE (micronized) 4.12%	Provides broad-spectrum sunscreen protection.
VITAMIN E (Tocopherol) 3.6%	Smoothes and hydrates.
EXTREMOZYMES® 3.0%	Protect & repair collagen and DNA against UVA and UVB damage.
ALOE 1.0%	Smoothes and hydrates Anti-inflammatory agent that promotes wound healing, collagen synthesis and wound maturation; has antimicrobial properties.
OLIVE LEAF EXTRACT 1.0%	Helps protect and repair.
CENTELLA ASIATICA (gotu kola) 0.75%	Potent antioxidant that stimulates collagen synthesis and improves microcirculation, capillary flow and vascular tone. Promotes wound healing and reduction of scar tissue.

Stockist Enquiries: isclinical.co.uk. For further information, images and samples please contact
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